[Second Edition.]

PATENT SPECIFICATION

466,548

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COMPLETE SPECIFICATION.

Process for the Manufacture of Lævo-ascorbic Acid (Vitamin-C).

I, TADEUS REICHSTEIN, Doctor of Technical Sciences, chemist, of No. 29, Hadlaubstrasse, Zurich, Switzerland, a citizen of the Swiss Confederation, do hereby declare the nature of this invention and in what manner the same is to be performed, to be particularly described and ascertained in and by the following statement:—

The physiologically important lævo-ascorbic acid has recently been prepared synthetically from lævo-xylosone (=lævo-lyxosone) by reaction with prussic acid followed by acid saponification. It was identical with the natural body and proved to be biologically active Vitamin-C (Specification number 425,198; Helvetica Chimica Acta vol. 16, 1933, page 1019).

This first process has the advantage of being generally applicable; it has so far in all investigated cases yielded the corresponding 3-keto-acids or their anhydrides. For the preparation of lævo-ascorbic acid in particular, however, there is the disadvantage that the starting material, lævo-xylosone, is obtainable only with difficulty and by expensive means. The search for a technically better method has led to the discovery of another way. According to this new method lævo-ascorbic acid is obtained by treating 2-keto-lævo-gulonic acid, in some cases after previous esterification, first with alkaline agents suitable for enolization and then with strong acids (Specification number 428,814). Instead of with alkaline agents the transformation of the 2-keto-lævo-gulonic acid may be carried out by heating at an acid reaction (Specification number 428,815). The heating of the 2-keto-lævo-gulonic acid or its derivatives which are easily split with acids is performed in aqueous or alcoholic solution. The transformation in alcoholic solution is specially described in Specification 459,207.

It has now been found that it is particularly advantageous to carry out the transformation of the 2-keto-lævo-gulonic acid and its derivatives which are easily split with acids in the presence of indifferent diluents in which lævo-ascorbic acid is difficultly soluble, such as chloroform, dioxane and the like.

EXAMPLE 1.

In a mixture of 200 parts by volume of chloroform and 37.5 parts by volume of ethyl alcohol (94%) 6 parts by weight of gaseous hydrogen chloride are dissolved, then 100 parts by weight of diacetone-2-keto-lævo-gulonic-acid-hydrate are added and boiled for 50 hours under reflux with stirring. The diacetone-keto-gulonic acid first goes into solution, but after a few hours the separation of the difficultly soluble ascorbic acid contained in the mixture of chloroform and alcohol already begins. After the time mentioned it is filtered off and washed with a mixture of chloroform and alcohol, 52 parts by weight of ascorbic acid being thus obtained. By titration with iodine the purity of this product is shown to be 96—97%. The yield, therefore, amounts to more than 80% of the theoretical. Only small quantities of ascorbic acid are contained in the dark-coloured mother liquor.

EXAMPLE 2.

35 parts by weight of 2-keto-lævo-gulonic-acid-methyl-ester are boiled for 70 hours while stirring under reflux in a mixture of 80 parts by volume of chloroform and 20 parts by volume of 15% alcoholic hydrogen chloride. 20.5 parts by weight of ascorbic acid are obtained of a purity of 97.3%, determined by titration with iodine.

EXAMPLE 3.

20 parts by weight of diacetone-2-keto-lævo-gulonic-acid-hydrate are dissolved in 60 parts by volume of dioxane. 5 parts by volume of concentrated aqueous hydrochloric acid are added and boiled under reflux. After boiling for three hours titration of the solution with iodine indicates that 65% of the theoretical quantity have been formed. The isolation of the ascorbic acid can be effected by evaporation in vacuo and stirring the residue into a paste with absolute alcohol, or by adding chloroform to the solution of dioxane.

Having now particularly described and

ascertained the nature of my said invention, and in what manner the same is to be performed, I declare that what I claim is :—

1. The process for the manufacture of lævo-ascorbic acid (Vitamin-C), which consists in heating 2-keto-lævo-gulonic acid or its derivatives which are easily split with acids in the presence of indifferent diluents in which lævo-ascorbic acid is difficultly soluble at an acid reaction.

2. The lævo-ascorbic acid (Vitamin-C), when prepared by the process claimed in claim 1.

Dated the 28th day of October, 1936.

TADEUS REICHSTEIN.

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